AΓ)	

Award Number: DAMD17-02-2-0022

TITLE: Military-Relevant Infectious Diseases Endemic to Kenya-Epidemiology, Immunology, Pathophysiology, Treatment and Prevention

PRINCIPAL INVESTIGATOR: Davey K. Koech, Ph.D.

CONTRACTING ORGANIZATION: Kenya Medical Research Institute

Nairobi, Kenya

REPORT DATE: March 2003

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;

Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 074-0188

maintaining

this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for

1. AGENCY USE ONLY (Leave blank) 2. REPORT DATE March 2003 3. REPORT TYPE AND DATES COVERED Annual (1 Mar 2002 - 28 Feb 2003)	reducing this burden to Washington Headquarters Ser Management and Budget, Paperwork Reduction Proje
4.TITLE AND SUBTITLE Military-Relevant Infectious Diseases Endemic to Kenya- Epidemiology, Immunology, Pathophysiology, Treatment and Prevention 6.AUTHOR(S) Davey K. Koech, Ph.D. 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 5. FUNDING NUMBERS DAMD17-02-2-0022 8. PERFORMING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
Military-Relevant Infectious Diseases Endemic to Kenya- Epidemiology, Immunology, Pathophysiology, Treatment and Prevention 6. AUTHOR(S) Davey K. Koech, Ph.D. 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 DAMD17-02-2-0022 DAMD17-02-2-0022 10. SPONSORING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	(Leave blank)
Epidemiology, Immunology, Pathophysiology, Treatment and Prevention 6. AUTHOR(S) Davey K. Koech, Ph.D. 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 8. PERFORMING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	4. TITLE AND SUBTITLE
Prevention 6. AUTHOR(S) Davey K. Koech, Ph.D. 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 8. PERFORMING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
6. AUTHOR(S) Davey K. Koech, Ph.D. 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 8. PERFORMING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
Davey K. Koech, Ph.D. 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 8. PERFORMING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	Prevention
Davey K. Koech, Ph.D. 7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 8. PERFORMING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	AUTHOR(S)
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 8. PERFORMING ORGANIZATION REPORT NUMBER 10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING	bavey k. koech, Fh.b
Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING	
Kenya Medical Research Institute Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING	
Nairobi, Kenya E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING	
E-Mail: smartin@nairobi.mimcom.net 9. SPONSORING / MONITORING	•
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012	Nairobi, Kenya
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012	
AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012 AGENCY REPORT NUMBER	E-Mail: smartin@nairobi.mim
U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012	
Fort Detrick, Maryland 21702-5012	AGENCY NAME(S) AND ADDRESS
11. SUPPLEMENTARY NOTES	Fort Detrick, Maryland
11. SUPPLEMENTARY NOTES	
	11. SUPPLEMENTARY NOTES
12a. DISTRIBUTION / AVAILABILITY STATEMENT 12b. DISTRIBUTION COD	
Approved for Public Release; Distribution Unlimited	Approved for Public Rele
13. ABSTRACT (Maximum 200 Words)	
Major expansion in personnel and infrastructure took place in the first year of this Cooperative Agreement. Clinical research facilities for the evaluation of drugs and vaccines for malaria and HIV/AIDS are under construction in Kisumu and Kericho, respectively. A Phase I trial (MAL-024) in 40 malaria-exposed adults, demonstrated that MSP-1, was safe, well tolerated and immunogenic in this population. It also demonstrated that complex clinical trails can be successfully undertaken in our field sites. Laboratory studies demonstrated differences in the level of expression of CR1 and CD55 in children with severe malarial anemia and cerebral malaria versus their respective controls. Studies also showed an age-dependent pattern of expression of RBC complement regulatory proteins which increase from childhood to adulthood and that children with severe	acilities for the evaluation of drugs espectively. A Phase I trial (MAL mmunogenic in this population. It ites. Laboratory studies demonstra nalarial anemia and cerebral malar

malaria have increased levels of immune complexes on their erythrocytes. Preparation for evaluating novel drugs and vaccines for HIV/AIDS was undertaken. Local HIV clades were characterized and incidence levels determined. In addition, ARV protocols and networking with local health programs were initiated. The Molecular Malaria Laboratory conducted research aimed at understanding the molecular mechanisms of drug resistance. Identification of mutations that confer resistance will allow assessment of the severity of drug resistant malaria and provide indications as to the effectiveness of current and future anti-malaria therapies. The combined vector, environmental, and map database were used to address questions about malaria transmission focality. Maps of the site were constructed using the differential global positioning system (GPS). On-site mosquito collections provided data for Entomological Inoculation Rates (EIRs) which indicated that the highest monthly EIR was 0.14, or an infective bite every three days in May. It was also determined that An. funestus tend to seek blood meals earlier than infective An. gambiae. This finding will have significant impact on transmission, and on assessment of disease risk since early biting infective vectors are more likely to find unprotected hosts.

14. SUBJECT TERMS malaria; HIV/AIDS; epidemiolo	15. NUMBER OF PAGES 15		
vectors; vaccine; anemia; anti-n	16. PRICE CODE		
17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

Table of Contents

Cover

SF 298

Table of Contents

Department of Malaria Immunology	page 1
Malaria Pathogenesis-1	page 2
Malaria Pathogenesis-2	page 4
Department of Anti-malarial Drug Discovery	page 4
Department of Entomology	page 5
Department of HIV/AIDS	page 6
Personnel and Training	page 9

Military-Relevant Infectious Diseases Endemic to Kenya: Epidemiology, Immunology, Pathophysiology, Treatment and Prevention. DAMD17-02-2-0022

Annual Report MAR 2001 to March 2002

PROGRAMS:

Department of Malaria Immunology

Chief: COL Jose Stoute

Malaria Clinical Trials LTC Mark Withers Background

Plasmodium falciparum malaria causes more than 1 million deaths per year. In lowland holoendemic areas of sub-Saharan Africa, such as in western Kenya, it is the children who bear the brunt of the morbidity and mortality due to malaria. Malaria in western Kenya is holoendemic. Malaria transmission occurs all year but at a very high level during the two rainy seasons. The adult population of several villages not far from the study site has been subject of several malaria chemotherapy and epidemi-ology studies. These studies typically demonstrate about 90% incidence of parasitemia over 12 weeks during a high transmission period.

The Walter Reed Project (WRP) and the Kenya Medical Research Institute (KEMRI) have been involved in malaria research in western Kenya for many years. These studies cover nearly every aspect of the disease: epidemiology, entomology, immunology, hospital-based treatment trials, and community-based studies of antimalarials. The WRP/KEMRI laboratories near Kisumu have served as the base for both phase I and II trials of candidate malaria vaccines and antimalarial drugs over the past decade. In spite of these research efforts, malaria infections in this area continue unabated and improved control strategies are required.

Worldwide, the populations at risk for malaria include not only the infants, children and adults in malaria-endemic regions, but also non-immune travelers to malarious areas including vacationers and deploying military personnel. A safe and effective vaccine that prevented infection, or even merely clinical symptoms, of *P. falciparum* malaria would be a milestone public health achievement and would become a mainstay in efforts to control this most serious infectious disease around the world. The increasing prevalence of drug resistance in various malaria strains makes an effective vaccine an international priority in the struggle for control of this devastating disease.

The target population for this particular vaccine is children at risk for clinical disease (including severe disease) due to infection with *P. falciparum*. MSP-1 can only be tested for proof of concept in this population, as there is no predictive animal model and no reliable challenge system to detect efficacy against clinical malaria. This vaccine has been tested in malaria naïve adults (US) to establish safety, reactogenicity and to

identify a dose for further evaluation. It was subsequently evaluated in malaria-exposed adults (Kenya) & has been found to be safe, well tolerated & immunogenic in this population. The next logical step in the clinical development of FMP-1/AS02A is its introduction into the pediatric population in a cautious, step-wise manner.

Accomplishments:

- 1. Successfully negotiated and launched a 4-year, \$2.8 million cooperative agreement with the Malaria Vaccine Initiative (Gates Foundation), GalaxoSmithKline and the USAID to pursue clinical field trials of MSP-1 in this malaria holoendemic area.
- 2. In a Phase I trial (MAL-024) in 40 malaria-exposed adults, demonstrated that MSP-1, was safe, well tolerated and immunogenic in this population. Also demonstrated that the present Kenyan and American team is capable of successfully undertaking complex clinical trails in this field setting.
- 3. Broke ground in March and took possession in October 2002 of a 9,000 sq ft clinical research facility in Kombewa in anticipation/support of many years of malaria vaccine & drug clinical trials.

Publication:

Withers, MR, JA Stoute, JA Gombe, et al., "Double-blind randomized safety and immunogenicity trial of *Plasmidium falciparum* MSP-1₄₂ adjuvanted in AS02A vs. rabies vaccine in malaria-experienced adults in western Kenya" [Abstract 331], *Program and Abstracts of the 51st Annual Meeting of the American Society of Tropical Medicine and Hygiene*, 67(2), Aug 2002.

Malaria Pathogenesis - 1 COL Jose Stoute Background:

Plasmodium falciparum malaria causes more than 1 million deaths per year. Most of these deaths occur as the result of complications such as severe malarial anemia and cerebral malaria. In lowland holoendemic areas of sub-Saharan Africa, such as in western Kenya, it is the children who bear the brunt of the morbidity and mortality due to malaria. Here, the most common complication is severe malarial anemia that occurs from a few months after birth, when transplacental immunity begins to wane, up to 24 months of age. Cerebral malaria is relatively rare in holoendemic areas and, when it occurs, it is usually seen in 2 to 5-year-olds. Adults are not as susceptible as children due to the acquisition of immunity after prolonged exposure. By contrast, in areas of the world with low transmission severe malarial anemia is still confined to young children but cerebral malaria makes up a larger proportion of the cases of severe malaria and is more common in older children and adults. Our research program aims to increase our understanding of the pathogenesis and the contrasting epidemiology of these two conditions.

To understand the pathogenesis of severe malarial anemia, we have examined the role of RBC complement regulatory proteins in malaria. Complement receptor 1 (CR1, CD35), decay accelerating factor (DAF, CD55), and membrane inhibitor of reactive lysis (MIRL, CD59) are RBC surface proteins that promote the inactivation and binding of C3b in immune complexes (ICs) (CR1), promote inactivation of C3b convertases (CD55), and interfere with the assembly of the membrane attack complex C5b-9 (CD59). Consequently, complement regulatory proteins may play an important role in protecting RBCs from complement activation and IC formation that occurs during malaria infection. In support of this hypothesis, work from our laboratory has shown that RBCs of children with severe malarial anemia are deficient in the complement regulatory proteins CR1 and CD55 (1, 2).

In addition to its potential role in the development of severe malarial anemia, CR1 has been implicated in the pathogenesis of cerebral malaria. RBCs infected with mature malaria parasites (trophozoites and schizonts) form rosettes by binding to CR1 present on the surface of uninfected RBCs. As the number of CR1 molecules on RBCs increases, so does their propensity to form rosettes. Rosette formation has been linked to the development of cerebral malaria, as it is more common in parasite cultures from patients with cerebral malaria than in cultures from patients with uncomplicated malaria. Rosettes are thought to play a role in the pathogenesis of cerebral malaria by plugging cerebral capillaries thereby interfering with cerebral blood flow.

Accomplishments:

- 1. Demonstrated differences in level of expression of CR1 and CD55 in children with severe malarial anemia and controls, and children with cerebral malaria and controls (1, 2).
- 2. Showed that RBC complement regulatory proteins have an age-dependent pattern of expression increasing from childhood to adulthood (Manuscript in preparation).
- 3. Showed that children with severe malaria have increased levels of immune complexes (Manuscript in preparation).
- 4. Showed that monocytes from children with cerebral malaria have high level of expression of the complement receptor 3 (Manuscript in preparation).
- 5. Obtained 4-year NIH grant to study the pathogenesis of severe malarial anemia.
- 6. Obtained 4-year training grant from the Fogarty International Center to support the training of 3 Kenyan Ph.D. candidates.

Publications:

- 1. Waitumbi JN, Opollo MO, Muga RO, Misore AO, Stoute JA. Red cell surface changes and erythrophagocytosis in children with severe *Plasmodium falciparum* anaemia. Blood 2000; 95:1481-6.
- Stoute JA, Odindo AO, Owuor BO, Mibei EK, Opollo MO, Waitumbi JN. Loss of RBC complement regulatory proteins and increased levels of circulating immune complexes are associated with severe malarial anemia. J Infect Dis. In press.

Malaria Pathogenesis -2 Dr. John Waitumbi

Background:

Non-immune patients infected with *P. falciparum* develop varying levels of disease severity. In the individuals who develop severe malaria, one of the most obvious parameter that is associated with severity is the level of parasite density. In absence of specific anti-parasitic immune responses in non-immune individuals, it is reasonable to assume that certain strains of *P. falciparum* cause severe disease because they have an imbalance between cell proliferation and cell loss. This assumption is strengthened by observation: 1) chemoprophylaxis that solely limits parasitemia reduces morbidity and mortality and 2) the in vitro growth rate between strains differ. Thus, understanding the basic mechanisms that underlie cell death may point to potentially new targets of therapeutic interventions to slow cell proliferation. One of the physiological mechanisms of reducing cell numbers is by apoptosis. Apoptosis is an active biochemical process that involves changes on three essential cellular components, namely, DNA, protein and lipid and once initiated irreversibly commit cells to death.

The molecular mechanisms involved in apoptosis are complex but they eventually involve DNA fragmentation, activation of caspaces and externalization of phosphatidylserine (PS). DNA double strand cleavage in apoptotic cells occurs at the linker regions between nucleosomes to produce fragments that are multiples of approximately 185 bp. These fragments can easily be demonstrated by agarose gel electrophoresis as characteristic ladders. *De novo* protein synthesis and/or the modification of existing proteins (such as caspaces) is another important attribute of apoptosis. Finally, lipids are also involved and several apoptotic pathways use signal-transduction systems based on membrane receptors and membrane-derived phospholipid precursors as second messengers.

This study proposes to determine whether there are fundamental differences in the apoptotic processes between strains of *P. falciparum* that maintain low parasite densities and those that maintain high parasite densities as measured by cell cycle distribution of DNA, DNA fragmentation and externalization of PS.

Accomplishments:

1. Established two *P. falciparum* cell lines with differential growth doubling time: These PF strains will be used to study whether apoptosis is involved in growth rate regulation.

Trainees:

PhD candidate thesis - The role of apoptosis in regulating *P. falciparum* cell numbers in non-immune individuals.

Department of Anti-malarial Drug Discovery

CPT Norman Waters

Background:

Our scientific research is conducted in two separate laboratories with distinct but complimentary efforts. The Malaria Drug Screening Laboratory conducts research aimed malaria drug discovery and drug resistance. Malaria drug discovery efforts currently test natural products, both as plant extracts and purified compounds, for their ability to kill the malaria parasite in culture. These efforts are aimed at identifying a naturally produced compound that can be transitioned into advanced development as a new anti-malarial drug. Drug resistance research is in support of the USAMRU-K GEIS program which has identified several geographically distinct areas of Kenya and Uganda where malaria parasites are collected, transported to the laboratory, and tested against a panel of 15 known anti-malarial drugs for their drug susceptibility profiles. This laboratory also will support malaria drug clinical trials with the culturing and testing of field isolates of malaria. The Molecular Malaria Laboratory conducts scientific research aimed at understanding the molecular mechanisms of drug resistance. Several genes are well characterized as obtaining mutations that confer resistance to several currently prescribed anti-malarial drugs. Identification of these mutations allows our laboratory to assess the severity of drug resistant malaria and provide indications as to the effectiveness of current and future anti-malaria therapies. This laboratory also conducts basic science projects aimed at identify malaria enzymes that can be targeted for drug discovery.

Department of Entomology. (STEP I. U):

MAJ Michael Sardelis

Background:

In FY02, the Entomology program at USAMRU-Kenya supported three primary research programs in Kenya. These programs covered malaria research in western Kenya and the city of Nairobi and arbovirus vector research along the coast of Kenya. Approximately 40 casual (full-time) employees were hired to assist in these programs and two vehicles were dedicated for support of the entomology project in western Kenya. An entomology laboratory was established at headquarters in Nairobi that supports specimen identification, storage (-70°C freezers), and PCR capabilities.

The project in western Kenya was designed to study the ecology of malaria vectors with the use of remote sensing and GIS to develop a new dry season malaria vector control strategy in Kenya. The combined vector, environmental, and map database were used to address questions about malaria transmission focality. Maps of the site were constructed using the differential global positioning system (GPS). The maps include permanent water sources and areas to find malaria vector eggs during the dry season. On-site mosquito collections provided data for Entomological Inoculation Rates (EIRs) which indicated that the highest monthly EIR was 0.14, or an infective bite every three days in May. It was also determined that An. funestus tend to seek blood meals earlier than infective An. gambiae. This finding will have significant impact on transmission, and on assessment of disease risk since early biting infective vectors are more likely to find

unprotected hosts.

In Nairobi, a malaria vector surveillance program was established in the Kibera shantytown, a district of the city with >700,000 inhabitants. Urban malaria is having an increasing impact in sub-Saharan Africa and in Nairobi the ecology is further confounded by the fact that the city is at an altitude of approximately 1 mile. Two of the most important vectors, *An. gambiae* and *An. arabiensis*, were found throughout the year in Kibera although at extremely low population densities. It appears that during the drier seasons these vectors are breeding in polluted streams that border the edge of the shantytown. No infected vectors were collected; however, our collections were associated with areas of suspected local transmission (based on travel histories of infected people).

Recent data from the Coast Province indicated ongoing dengue transmission. An arbovirus surveillance program was established that initially focused on vector surveillance in the localities of the identified infections. Household vector surveillance was conducted throughout the year and collected eggs from ovicups to determine the presence/absence of the vector in the area. Aedes aegypti is the primary dengue vector but other potential vector species are present. Ae. aegypti is not usually found indoors although larvae are quite abundant especially during the rainy seasons. Temperature and humidity data for the study area was collected. A human use protocol for a dengue serosurveillance study was submitted through KEMRI. Potential study sites were identified in Mombasa and Malindi. In addition to these studies, entomology provided support for CONUS based programs to include phase one of the Dengue Vector Control System device testing. This was a 15 week test program designed to evaluate the effectiveness of traps for collecting dengue vectors. Support was also provided for several leishmaniasis programs/protocols.

Department of HIV/AIDS (STEP H.)

MAJ(P) Ginamarie Foglia

Background:

The United States Military HIV Program, also known as The Walter Reed Project, was established by the joint collaboration of the Walter Reed Army Institute of Research and The Henry M. Jackson Foundation in Washington, D.C., U.S.A. The United States Army Medical Research Unit – Kenya (USAMRU-K) is the primary field station for U.S. medical research in Kenya. USAMRU-K provides regional coordination between our programs in Uganda, Tanzania, and Kenya. The primary mission of the Project is to develop strategies to prevent HIV infection globally. The primary objective of this effort is establishing a vaccine for HIV. The current rationale is to develop vaccines based on the genetics and subtypes or clades of the viruses prevalent in different regions of the world. The program is already advancing a second-generation, clade E vaccine strategy to efficacy testing in Thailand, where clade E is most prevalent. Clinical testing of vaccines in East Africa permits evaluation of the role of genetic diversity as clades A, C, and D are contributing in varying proportions to the HIV epidemic in the region.

A key element in developing a vaccine is to appropriately identify cohorts in which to conduct vaccine trials. Current studies are designed to develop a cohort in an agricultural setting in the highlands of western Kenya. Specifically, the Project's objectives are to: (1) estimate the incidence and prevalence of HIV, (2) characterize the risk factors associated with HIV infection, (3) determine the viral clade and recombinations of HIV-1 in this part of Kenya, (4) characterize the kinetics of HIV-specific immune responses, CD4 counts and viral loads in early HIV infection and in the face of malaria co-infection, and (5) characterize the drug resistance patterns of Plasmodium species.

In addition to conducting research, the Program also sponsors HIV prevention programs. Currently, we are actively educating the local communities about HIV through "barazas" where our staff perform drama relating to HIV risk behaviors and illness in Kiswahili and English. Our Program Football Team interacts with the community players and give pregame HIV education in the form of Kiswahili literature, "rapping", and distributing condoms. The Program conducts workshops to update the local medical community and facilitates the development of other prevention programs such as mother-to-child transmission and HIV in the workplace. The Boston University School of Public Health started collaborating with the Program last year to estimate the impact of morbidity on labor productivity in the Kenya Highlands. Additionally, we have begun construction of new HIV research and counseling facilities at the district hospital in April 2003, where regular training for counselors and healthcare providers will be sponsored.

Previous, completed studies have included a blood bank collection, a trial of a new diagnostic assay, and a pilot epidemiological survey. The collection of discarded HIV positive blood bank units from across the country has created an archive of large volumes of plasma and peripheral blood mononuclear cells from 500 anonymous individuals, which is currently being used to full-length sequence the virus from all over the country.

ACCOMPLISHMENTS:

- 1. Completed Good Laboratory Practice training for over 200 African researchers and staff in May 2002 at Nairobi, Kenya.
- 2. Completed Good Clinical Practice training for over 200 African researchers and staff in September 2001 at Nairobi, Kenya.
- 3. Began HIV Productivity Study in collaboration with Boston University School of Public Health in 2002.
- 4. Began administering Nevirapine through collaboration with the Elizabeth Glaser Pediatric AIDS Foundation Grant of \$210,000 at Kericho hospitals to HIV-infected mothers and their babies to prevent vertical transmission of HIV in October 2002. Awarded grants in 2002 and 2003 to procure free Determine HIV Rapid Tests and Nevirapine tablets to facilitate the Prevention of Mother to Child Transmission of HIV at several Kericho sites.
- 5. Completed seminar on antiretroviral therapy for the Kericho branch of the Kenya Medical Association in 2001.

- 6. Trained local Kericho and Program Medical Officers in Antiretroviral Medication Administration and Monitoring in September 2002 through Ecumenical Pharmaceutical Network and Mission for Essential Drugs and Supplies.
- 7. Instituted community programs for voluntary counseling and testing in 2000-present.
- 8. Developed HIV Postexposure Programs (PEP) for Kericho Hospitals and sponsored training of their Medical Officers supervising PEP in September 2002. This PEP has been successfully transferred to the US Military HIV Program in Uganda and Tanzania.
- Granted AIDS Vaccine Advocacy Coalition (AVAC) funding to purchase essential medical equipment for the Kericho District Maternity and Delivery Wards in January 2003 to help prevent the transmission of HIV from mother to child.
- 10. Donate essential medications to local Kericho hospitals.
- 11. Trained Kericho Laboratory Staff in IATA regulations regarding shipping infectious/biological materials in 2003.
- 12. Commenced "HIV and Malaria Cohort Study Among Plantation Workers in Adult Dependants in Kericho, Kenya" protocol WRAIR #855 in June 2003.
- 13. Began Proficiency Testing in January 2003 of all rapid HTV tests to maintain quality assurance and control at all laboratory sites involved in the Elizabeth Glaser Pediatric AIDS Fund for Prevention of Mother to Child HTV Transmission (PMTCT).
- 14. Mentored Global Emerging Infectious Disease Surveillance Program USU Medical Students/Residents during their Kenya rotations.
- 15. PMTCT Program trained over 50 Kericho district mid-wives, medical/clinical officers and nurses in HIV voluntary HIV testing and counseling and prevention of mother to child transmission of HIV in May June 2003.
- 16. Commenced construction of 7,500 square foot state-of-the-art laboratory at Kericho District Hospital in April 2003 to be used for future HIV vaccine research. Completion scheduled for late November 2003.
- 17. Commenced construction of 4,000 square foot Maternal Child Health Clinic at the Kericho District Hospital in April 2003 to be used for PMTCT activities. Completion scheduled for late November 2003.

Military-Relevant Infectious Diseases Endemic to Kenya:Epidemiology, Immunology, Pathophysiology, Treatment and Prevention. DAMD17-02-2-0022

Annual Report MAR 2001 to March 2002

PERSONNEL AND TRAINING

No.	Grade	P/No	Employee Name	DESIGNATION		
	MR			ADMINISTRATION	On Training	Course
1	11	80182	Kadenge Kidiga	Senior Accountant	-	
2	10	80057	Fred Kiddy Onyango	Senior Lab Technologist		
3	9	80079	Joyce Mburu	Personal Secretary		
4	9	80134	Lucy Lodenyi	computer Programmer I		
5	9	80231	Raphael Pundo Omondi	Computer Programmer I	On Training	MSC
6	9	80253	Dickens O. Atieno	Assistant Research Officer	On Training	MSC
7	9	80304	Caroline C. Tungwony Dishon Humphrey	Assistant Research Officer		
8	9	80329	Otieno	Accountant II		
9	8	80080	Daniel Waema	Supplies Officer III		
10	7	80250	Shadrack O. Odera	Computer Operator I		
11	7	20486	Nahashon G. Ngugi	Administrative Assistant		
12	6	80035	Agnes Nganga	Computer Operator II		
13	5	80206	John G. Kamau	Driver Grade I		
14	5	80262	Mildred Achieng	Copy Typist II		
15	4	80207	Edwin C. Mbwabi	Senior Auxiliary Staff		
16	3	80274	Jeconia O.Bunde	Auxilliary Staff I		
17	3	80277	Johnstone O Otieno	Driver Grade III		
18	3	80401	Charles O Gekondo	Auxilliary Staff I		
19	3	80389	Julius M Muhanji	Auxilliary Staff I		
20			Charles O Moranne			
			Casual hire	Seasonal		
				SUBTOTAL		
				Clinical Trials/Kombewa		
1	10	21545	Otieno Geoffrey A. Dr.	Assistant Research Officer		
2	10	21586	Odhala Joash Gombe Dr.	Assistant Research Officer	On Training	Mmed
3	10	80409	Oenga Ezekiel R. Dr.	Assistant Research Officer		
3	9	80247	Melanie Atieno Onyango	Assistant Research Officer		
3	9	80309	Achola N. Onyango	Administrativ Officer II		
3	9	80380	Paul O Jaleny	Assistant Research Officer		
3	7	80147	Charles Okundo Okelo	Laboratory Technician II		
4	7	80053	Ramadhan Mutalib	Laboratory Technician II		
5	7	80232	Gordon M. Hongo	Lab Technologist III		
6	7	80233	Joseph Ouya Osoga	Lab Technologist III		
7	7	80318	Agnes Owiti Akoth	computer Programmer I		
8	7	80377	Stacy M Okalo	Clinical Officer		
9	7	80382	Phoebe Muga Otieno	computer Programmer III		
10	7	80384	Rosemary O Opiyo	Enrolled Nurse III		
11	6	80049	Nerry Oluoch Ndiege	Laboratory Technician III		

12		80042	Samwel Odour Wangowe	Junior Lab. Technician	
13	6	80362	Dickson Amollo	Lab Technitian III	
14	6	80386	Imelda A Adongo	Enrolled Nurse III	
15	6	80368	James S Odera	Lab Technitian III	
16	6	80371	Kennedy J Obonyo	Lab Technitian III	
17	6	80381	Peter R Mariga	Senior Driver	
18	6	80375	Veronica W Mungai	Pharmaceutical Tech	
19	5	80168	Abdi Ayub	Driver Grade I	
20	5	80374	Mary A Amondi	Computer Operator III	
21	4	80167	David L. Madahana	Driver Grade II	
22	4	80181	George Nyawade	Driver Grade II	
23	4	80045	Joram Osumo	senior Auxilliary Staff	
24	4	80061	Philistus Oigo Ogilo	senior Auxilliary Staff	
25	4	80054	Cyrus Ongonga Onguka	Senior Auxiliary Staff	
26	4	80353	Fred Antony Aketch	Clerical Officer	
27	4	80354	Beatrice O Akinyi	Clerical Officer	
28	4	80358	Clarice Ogendo Adhola	Clerical Officer	
29	4	80360	Daniel A. Odhiambo	Clerical Officer	
30	4	80361	Moses D Olweny	Clerical Officer	
31	4	80364	Elizabeth B Akinyi	Clerical Officer	
32	4	80365	Florence A Owak	Clerical Officer	
33	4	80366	George O Obilo	Driver Grade III	
34	4	80367	Jacob N Jagongo	Clerical Officer	
35	4	80369	Jane Atieno Ombayi	Clerical Officer	
36	4	80373	Lilian A Ooro	Clerical Officer ·	
37	4	80378	Milicent Awuor	Clerical Officer	
38	4	80379	Nelly A Owuondo	Clerical Officer	
39	4	80376	Wycliff H Odhiambo	Clerical Officer	
40	3	80165	Raphael onyango	Auxilliary Staff I	
41	3	80312	Ruth Awino Opiyo	Auxilliary Staff I	
42	3	80313	Charles Kangu Isiaho	Driver Grade III	
43	3	80385	Caroline Adhiambo	Auxilliary Staff I	
44	3	80356	Caroline Atieno	Auxilliary Staff I	
45	3	80355	Caroline A Onoka	Auxilliary Staff I	
46	3	80359	Daniel O Osewe	Auxilliary Staff I	
47	3	80363	Edward Mutoka	Driver GradeIII	
48	3	80387	Mathews O Okendo	Auxilliary Staff I	
49	3	80383	Robert O Ogutu	Auxilliary Staff I	
50	3	80357	Christabel A. Atieno	Auxilliary Staff I	
			Casual hire	Seasonal	
			X7	SUBTOTAL	
			Vaccine/Immnology Dr. John Njenga		
1	12	80241	Waitumbi	Senior research officer	
2	11	80068	Joseph Koros	Principal Lab. Technologist	
3	11	80246	Joram Ogola Siagla	Research officer	
4	11	21297	Eunita A Ohas	Research officer	
6	9	80273	Willis Okoth	Assistant Research Officer	
7	6	80244	James Gitonga	Laboratory Technician III	
8	4	80050	Consolata Onyango	senior Auxilliary Staff	
			Casual hire	Seasonal	
				SUBTOTAL	
			Severe Malaria		
1	11	80372	Lilian A Ogonda	Research officer	

. .

•

2	11 9	80388 80259	Dr.Walter Otieno Alfred Olweny Odindo	Research officer Clinical Officer I	On Training	MSC
4	9	80261	William O. Odhiambo	Assistant Research Officer		
5	9	80275	Boaz Owino Owuor	Assistant Research Officer	On Training	MSC
6	9	80307	Colins O. Odhiambo	Assistant Research Officer		
7	9	80308	Michael M. Odera	Assistant Research Officer		
8	7	80310	Titus o. Apindi	Laboratory Technologist III		
9	7	80164	Michael Ouma Opiyo	Laboratory Technologist III	On Training	HND
10	7	80260	Vincent Oloo Otieno	Clinical Officer III		
11	7	80255	David Ousu	Clinical Officer III		
12	6	80047	Dismas Achango	Laboratory Technician III		
13	6	80370	Kennedy O Dudi	Lab Technitian III		
14	3	80245	Maurice Odongo Otieno	Driver Grade III		
15	3	80263	Charles Otieno Adega	Auxilliary Staff I		
16	3	80311	Joseph Thomas Onyango	Driver Grade III		
17	8	80391	Fredrick M. Mucheru	Engineering Technitian		
				SUBTOTAL		
				RETROVIROLOGY		
1	11	80044	David Kiplangat Chumo	Principal Lab.Technologist		
2	10	80279	Dr. Dorothy W. Njeru	Assistant Research Officer		
3	10	80406	Koech Hillary K	Accountant 111		
4	9	80251	Lilian Chepkemoi	Assistant Research Officer	on Training	MSC
5	9	80281	Wilfred Langat	Public Health Officer		
6	9	80400	Bornes C.Korir	Assistant Research Officer		
7	7	80392	Loice C Cheruiyot	Lab Technologist III		
8	7	80330	Roseline Bosibori Vicky	Lab Technologist III		
9	6	80256	Maurice O. Onyango	Enrolled Nurse III		
10	6	80257	Michael O. Obonyo	Enrolled Nurse III		
11	5	80323	Everlyn Ngetich	Higher Clerical Officer		
12	5	80325	Judy Chebet Bosuben	Computer Operator III		
13	5	80332	Susan Adega	Computer Operator III		
14	4	80286	Vincent Oduur Osewe	Clerical Officer		
15	4	80282	Caleb Omware Achieng	Senior Auxillary Staff	on Training	Certificate
16	4	80285	Fredrick Ouma Waga	Clerical Officer	on Training	Certificate
17	4	80284	Francis Ochieng Opiyo	Clerical Officer	on Training	Certificate
18	4	80327	Peter Mikaye Ondieki	Clerical Officer		
			Roselidah Oyunga			
19	4	80328	Oyunga	Clerical Officer	on Training	HND
20	3	80283	George Odongo Okoth	Driver Grade III		
21	3	80316	David Kamadi Onyino	Driver Grade III		
22	3	80315	Johnson Ndungu Shiyai	Driver Grade III		
23	3	80314	Jude Kitur	Driver Grade III		
24	3	80324	James Obino	Auxilliary Staff I	on Training	Driving
25	3	80331	Samwel Obino	Auxilliary Staff I		
26	3	80322	Dennis Ouma Otieno	Auxilliary Staff I	on Training	Certificate
27		80393	Anthony A Keya	Assistant Cateress		
28		80394	Edna C Mutai	Auxilliary Staff I	on Training	Diploma
29		80395	David K Chirchir	Auxilliary Staff I		
30		80396	Eric K Rono	Lab Technologist III	on Training	Certificate
31		80397	Ignatius Kipnge'etich	Assistant Research Officer		
32		80398	Rachael K Kamau	Assistant Research Officer	on Training	HND
33		80399	Bernard Oronje	Auxilliary Staff I		
34		80402	Florence Malesi	Auxilliary Staff I		

8 - 3

35

80403 Pamela A Pande

Lab Technologist III

SUBTOTAL PMTCT

Casual hire

Seasonal

SUBTOTAL